EXHIBIT 45

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION This document relates to: *The County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al.* Case No. 18-op-45090 *The County of Cuyahoga, Ohio, et al. v. Purdue Pharma L.P., et al.* Case No. 17-op-45004	MDL No. 2804 Case No. 17-md-2804 Hon. Dan Aaron Polster

EXPERT REPORT OF MELANIE H. ROSENBLATT, M.D.
MAY 10, 2019

I. INTRODUCTION AND QUALIFICATIONS

A. Background and Qualifications

1. I am the Medical Director of Pain Management at Pain Management Strategies, Inc., the Medical Director of Acute Pain Management at Holy Cross Hospital, and a founding partner of Melrose Pain Strategies. Until 2017, I was the Medical Director of Pain Management for Broward Health North, a level II trauma center, where I was also the chairperson of the Credentials and Qualifications Committee and a member of the Medical Executive Board.

2. I completed my undergraduate education at the State University of New York at Stony Brook. I obtained my M.D. from the State University of New York at Stony Brook School of Medicine in 1991.

3. I completed my Anesthesiology residency and pain training at St. Joseph's Hospital Health Center in Syracuse, New York. I am board certified in Anesthesiology, Pain Management, and Addiction Medicine.

4. I have been active in several local, regional and national professional societies, including the American Society of Anesthesiologists, the Society for Pain Practice Management, the American Academy of Pain Management, and the American Society of Addiction Medicine.

5. I lecture nationally about safety and risk assessment in the treatment of chronic pain. My academic research and opinions on opioid use disorder and opioid tapering/withdrawing

have been published in Pain Medicine News and Future Medicine's Pain Management journal.[1]

6. I am an affiliate faculty member at the University of Miami as an educator in Pain Management. I was also a clinical instructor at Nova Southeastern University College of Osteopathic Medicine in the Department of Surgery.

7. I have extensive experience with the prescribing of Actiq and Fentora. This includes clinical experience gained in both the inpatient and outpatient setting. I have prescribed oral transmucosal fentanyl citrate medicines, including Actiq and Fentora, for indications listed and unlisted on the FDA-approved package insert.

8. I currently bill for my services at $600 per hour. My compensation for the work on this matter is not contingent upon the outcome of this litigation or on the content of the opinions that I offer in this case. Appendix A provides my Curriculum Vitae, which includes a list of my expert testimony within the past four years.

B. Assignment

9. I have been retained by counsel for Cephalon, Inc. ("Cephalon"), Teva Pharmaceuticals USA, Inc. ("Teva USA"), Actavis Pharma, Inc. ("Actavis Pharma"), Actavis LLC ("Actavis LLC"), Watson Laboratories, Inc. ("Watson"), and other affiliates[2]to serve as an expert witness in this case.

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[1] Pergolizzi, J. V., Jr. et al., "Tapering opioid therapy: clinical strategies," *Pain Management* Vol. 8, No. 6 (2018): 409-13.

[2] Teva USA and Cephalon are referred to as the "Teva Defendants." Actavis Pharma, Actavis LLC, Watson, Warner Chilcott Company, LLC, Actavis South Atlantic LLC, Actavis Elizabeth LLC, Actavis Mid Atlantic LLC, Actavis Totowa LLC, Actavis Kadian LLC, Actavis Laboratories UT, Inc. f/k/a Watson Laboratories, Inc.-Salt Lake City, and Actavis Laboratories FL, Inc., f/k/a Watson Laboratories, Inc.-Florida are referred to as the "Actavis Generic Defendants." In addition, I understand that Teva

treatment time, but also indirect costs. These indirect costs can include "lost income as a result of time taken off work for a [breakthrough pain] episode, a spouse's or caregiver's lost income because of time off work, or the expense of extra household help[, ...] the patient's pain, suffering, depression, anxiety, loss of sleep, and fatigue, as well as the family's and/or caregiver's distress."[38] Cancer patients with breakthrough pain have also been found to require more pain-related hospitalizations and physician office visits, leading to increased medical costs.[39] This is also consistent with my experience working with CNCP patients who have suffered from untreated or under-treated breakthrough pain.

VI. OPINION #3: OPIOIDS MAY BE AN APPROPRIATE TREATMENT OF CNCP FOR PATIENTS WHO ARE APPROPRIATELY SCREENED AND MONITORED. IN PARTICULAR, ACTIQ AND FENTORA MAY BE APPROPRIATE TREATMENTS OF BREAKTHROUGH CNCP FOR OPIOID-TOLERANT PATIENTS WHO ARE APPROPRIATELY SCREENED AND MONITORED.

37. Opioids have been used for the treatment of a variety of painful conditions, including acute pain following trauma or surgery, cancer-related pain, and CNCP.

[38] Abernethy, Amy P, Jane L Wheeler, and Barry V Fortner, "A health economic model of breakthrough pain," *American Journal of Managed Care* Vol. 14, No. 5, Supplement 1 (2008): S129-40.

[39] Fortner, Barry V, Theodore A Okon, and Russell K Portenoy, "A survey of pain-related hospitalizations, emergency department visits, and physician office visits reported by cancer patients with and without history of breakthrough pain," *The Journal of Pain* Vol. 3, No. 1 (2002): 38-44; Fortner, Barry V et al., "Description and Predictors of Direct and Indirect Costs of Pain Reported by Cancer Patients," *Journal of Pain and Symptom Management,* Vol. 25, No. 1 (2003): pp. 9-18, pp. 14-16 ("The presence of breakthrough pain was a significant predictor of direct pain-related costs [...] indicating that patients with breakthrough pain incurred higher direct pain-related costs [...] than patients without breakthrough pain. [...] The presence of breakthrough pain predicted higher indirect pain-related costs. [...] Pain intensity, pain interference, and presence of breakthrough pain predicted higher indirect expenses, suggesting that as pain intrudes on the daily lives of cancer patients they begin to incur expenses for issues outside of direct medical treatment of pain").

38. Short-acting opioids work to control pain regardless of the etiology of the pain. When used in combination with long-acting opioids, short-acting opioids are used to manage breakthrough pain. When short-acting opioids are used alone (not in combination with long-acting opioids), they can be effective for treating breakthrough pain, when a patient prefers to not be on opioids "around-the-clock." For example, patients may prefer not to be on opioids during the day when they have to be at work or need to care for children. In my experience, I have also found that people whose job consists of driving (e.g., delivery drivers, couriers, truck drivers) prefer not to be on opioid therapy while driving. Some of my patients experience more pain than usual after a particularly active day. In these circumstances, patients may benefit from short-acting opioids taken on an as-needed basis.

39. Long-acting opioids work continuously and are indicated for the management of chronic pain when other alternatives have failed and for which around-the-clock pain relief is needed.[40] Prescribing long-acting opioids can benefit a patient in a number of ways, including, but not limited to, maintaining a constant level of medication in the body, potentially preventing pain recurrence, and minimizing feelings of euphoria and/or withdrawal. Furthermore, patients may find it easier to comply with prescribing instructions for long-acting opioids, as they are associated with fewer administrations per day relative to short-acting opioids.

40. In my own practice, opioids play an important role in the chronic pain armamentarium. For example, when treating patients with chronic pain with no history of substance abuse,

[40] Ray, James B, "Implications of the extended-release/long-acting opioid REMS for managed care," *American Journal of Managed Care* Vol. 21 (2015): S177a-S187a.

I have found that some patients who remain in severe, debilitating pain following non-opioid treatment (such as ice, heat, or physical therapy) benefit from a trial of opioid therapy. In general, the suitability of long-acting opioids for chronic pain depends on the nature and intensity of a patient's pain, the patient's therapeutic goals, and the expected impact of treatment on his or her quality of life. Two patients suffering from similar levels of chronic pain may well benefit from different treatment strategies. The choice of non-opioid therapy for one does not diminish the potential efficacy of opioid therapy for the other. Many opioids have been and continue to be approved for the treatment of CNCP.[41]

41. Plaintiffs' experts appear to take different views on whether it is appropriate to use opioids to treat CNCP. Most agree that opioids have an important role to play in treating pain, but there is more variety in opinions about which cases are appropriate. I agree with Dr. Schumacher that opioids can be appropriate for treating conditions "such as pain from advanced multiple sclerosis, sickle cell disease, pain following spinal cord injury and paraplegia, or post-herpetic neuralgia [...as a] a third-line therapy" after other treatments have been attempted.[42] I also agree that opioids "have an integral role in the current practice of medicine," "have long been used successfully for the management of acute pain," and are appropriate for certain patients suffering from CNCP.[43] Other experts,

[41] Examples include Hysingla ER, Zohydro ER, or Vicodin. Hysingla ER's indications, for example, include "the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate." "Hysingla ER Label, September 2018," 2018, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206627s007s008lbl.pdf.

[42] Expert Report of Mark A. Schumacher, M.D., Ph.D., *In Re: National Prescription Opiate Litigation*, MDL No. 2804, March 25, 2019 ("Schumacher Report"), ¶ 86.

[43] Schumacher Report, at ¶¶ 86, 121, 140.

such as Dr. Lembke, assert that opioids have little to no role in treating chronic pain.[44] This wide disparity in the opinions of Plaintiffs' experts mirrors the wide range of opinions in the medical field. In my experience, strategies to manage chronic pain vary widely whereas strategies to manage other chronic medical conditions are generally more standardized.[45]

42. I agree that opioids carry significant safety risks, which are disclosed in the labels for the medicines and which are taught to all physicians in the course of their medical school and training. I also agree that opioids should not be the first-line treatment for CNCP or cancer pain. Nonetheless, opioids can be effective in treating CNCP, based upon my experience treating thousands of patients, both inpatient and outpatient, for acute and chronic pain.

43. Although non-pharmacologic and non-opioid pharmacologic therapies are preferred for both acute and chronic pain, opioids may be considered for patients that fail to respond to these more conservative therapies. In general, I use a multimodal approach to pain treatment that includes non-pharmacologic as well as non-opioid and opioid therapy. In doing so, I approach pain from multiple pathways (e.g., ice, heat, physical therapy, interventional pain techniques) and assess patient response. Depending on a patient's specific conditions, I sometimes try non-opioid medication as well, including muscle

[44] Expert Report of Anna Lembke, M.D., *In Re National Prescription Opiate Litigation*, MDL No. 2804, March 25, 2019 ("Lembke Report"), p. 5 ("Limiting opioid prescribing is good medicine, because it decreases exposure to a dangerous and potentially lethal drug, without compromising pain treatment. [...] there is insufficient evidence that long-term opioid therapy effectively treats chronic pain.").

[45] An article published by Multiple Chronic Conditions Resource Center suggests that "[b]ecause pain tolerance is different for every individual, there is no one-size-fits-all approach to chronic pain management." *See* Multiple Chronic Conditions Resource Center, "Chronic Pain Guidelines," available at https://www.multiplechronicconditions.org/chronic-pain-guidelines.

relaxants, anti-inflammatories, antidepressants, and anticonvulsants. When prescribing opioids as part of this comprehensive approach, I begin treatment with the lowest effective dose then continually assess the risks/benefits and monitor for side effects. Although there is no single formula or protocol for appropriate opioid prescribing, it is generally not acceptable to simply escalate the dose until side effects become problematic. Instead, I take into account the totality of each patient's response to multimodal therapy in making changes to their medications, as well as the risks and potential benefits of that such therapy.

A. Off-label Prescribing May be Appropriate for Treating CNCP

44. Physicians often use medications for purposes other than the FDA-approved indication.[46] This includes numerous medications that have been or are used for the treatment of pain, such as amitriptyline, trazodone, desipramine, imipramine, venlafaxine, gabapentin, oxcarbazepine, topiramate, or transdermal lidocaine patch. Many of these medicines were approved with a limited pain-related indication or no pain indication at all, but are frequently prescribed for off-label indications in patients experiencing CNCP. For example, trazodone, which is indicated only "for the treatment of major depressive disorder," can be an effective adjuvant for CNCP as well as comorbid anxiety, insomnia and depression.[47]

[46] A report of off-label prescribing patterns of US office-based physicians documented that 46% of prescriptions for cardiac and anticonvulsant medications were for off-label indications. Radley, David C, Stan N Finkelstein, and Randall S Stafford, "Off-label prescribing among office-based physicians," *Archives of Internal Medicine* Vol. 166, No. 9 (2006): 1021-26.

[47] Substance Abuse and Mental Health Services Administration (SAMHSA), "Managing Chronic Pain in Adults With or in Recovery from Substance Use Disorders," 2012, available at

45. Examples of common off-label use of medications in patients with pain include the use of gabapentin for a wide variety of neuropathic pain conditions, even though gabapentin is indicated only for the management of postherpetic neuralgia and epilepsy in adults.[48] Gabapentin has also been used as part of multi-modal pain therapy in patients following surgery. Tricyclic antidepressants have been used as a co-analgesic for the treatment of a wide variety of painful conditions, including fibromyalgia, neuropathic pain (including postherpetic neuralgia and painful diabetic peripheral neuropathy), and chronic low back pain.

B. Opioids May be an Appropriate Treatment for Breakthrough Pain

46. Patients who take around-the-clock opioids for CNCP often report experiencing breakthrough pain, including "end-of-dose failure" pain. Breakthrough pain occurs in approximately 50% of outpatients with both cancer and non-cancer pain.[49] Published clinical guidelines on the use of opioids for the treatment of CNCP recognize that breakthrough pain can occur in patients suffering from non-cancer pain.[50]

47. Breakthrough pain can be treated using rapid-acting opioids such as TIRFs. Actiq and Fentora are examples of TIRFs. These transmucosal opioids can be administered via

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https://store.samhsa.gov/system/files/sma13-4671.pdf; "Trazodone Label," 2015, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/071196s062lbl.pdf.

[48] "Neurontin (Gabapentin) Label," 2017, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020235s064_020882s047_021129s046lbl.pdf.

[49] Rudowska, "Management of breakthrough pain due to cancer," *Contemporary Oncology* Vol. 16, No. 6 (2012): 498-501, p. 1; Portenoy et al., "Breakthrough pain in community-dwelling patients with cancer pain and noncancer pain, part 1: prevalence and characteristics," *Journal of Opioid Management* Vol. 6, No. 2 (2010): 97-108.

[50] Chou, Roger et al., "Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain," *The Journal of Pain* Vol. 10, No. 2 (2009): 113-30.e22, pp. 122-123.

intranasal sprays, sublingual sprays, and sublingual tablets. TIRFs become active within minutes and have a duration of 1-2 hours, which correspond well to the time course of breakthrough pain. Longer-acting opioids may not be as effective for managing breakthrough pain due to their delayed onset, as there is an urgency to treating breakthrough pain. TIRFs can be also beneficial for those who do not tolerate oral medications. During end-of-life care, up to 70% of patients require a non-oral route of opioid administration. Buccal absorption from crushed pills can pose a choking hazard (and are not indicated for use in this manner). Thus, TIRFs are a noninvasive, effective, and efficient way of administering pain relief.[51] As noted above, physicians must weigh the potential benefits with risks of harm when considering the use of rapid-acting opioids for the treatment of breakthrough pain in patients.

48. Studies have found that TIRFs (including sublingual sprays and sublingual fentanyl tablets) are efficacious in treating breakthrough cancer and non-cancer pain in patients who are opioid tolerant.[52] Patients with chronic cancer and non-cancer pain have been

[51] Chang, Andrew et al., "Transmucosal immediate-release fentanyl for breakthrough cancer pain: opportunities and challenges for use in palliative care," *Journal of Pain & Palliative Care Pharmacotherapy* Vol. 29, No. 3 (2015): 247-60.

[52] See, e.g. Shimoyama, N. et al., "Efficacy and safety of sublingual fentanyl orally disintegrating tablet at doses determined from oral morphine rescue doses in the treatment of breakthrough cancer pain," *Japanese Journal of Clinical Oncology* Vol. 45, No. 2 (2014): 189-96; Nalamachu, Srinivas et al., "Long-term effectiveness and tolerability of sublingual fentanyl orally disintegrating tablet for the treatment of breakthrough cancer pain," *Current Medical Research and Opinion* Vol. 27, No. 3 (2011): 519-30; Minkowitz, Harold et al., "Long-term safety of fentanyl sublingual spray in opioid-tolerant patients with breakthrough cancer pain," *Supportive Care in Cancer* Vol. 24, No. 6 (2016): 2669-75; Mercadante et al., "Factors influencing the use of opioids for breakthrough cancer pain: A secondary analysis of the IOPS-MS study," *European Journal of Pain* Vol. 23, No. 4 (2018): 719-26; Webster, Lynn R et al., "Fentanyl buccal tablet compared with immediate-release oxycodone for the management of breakthrough pain in opioid-tolerant patients with chronic cancer and noncancer pain: a randomized, double-blind, crossover study followed by a 12-week open-label phase to evaluate patient outcomes," *Pain Medicine* Vol. 14, No. 9 (2013): 1332-45; Ashburn, Michael A et al., "The efficacy and safety of fentanyl buccal tablet compared with immediate-release oxycodone for the management of breakthrough pain in opioid-tolerant patients with chronic pain," *Anesthesia & Analgesia* Vol. 112, No. 3 (2011): 693-702; Taylor et al., "Impact of breakthrough pain on quality of life in patients with chronic, noncancer pain: Patient perceptions and effect

found to prefer fentanyl buccal tablets over oxycodone, and both patients and clinicians have reported better functional improvements with fentanyl buccal tablets, versus other short-acting opioids.[53] Patients with chronic pain have also reported greater pain reduction after fentanyl buccal tablets versus oxycodone.[54]

49. In particular, clinical studies have also found that Actiq and Fentora are effective in treating breakthrough pain. One study of the effect of treatment with OTFC medicines found that Actiq (and similar medications) resulted in substantial improvement in several quality of life metrics, including "general activity level."[55] Another study found that Actiq yielded significantly better pain reduction than immediate-release morphine sulfate in those with breakthrough cancer pain.[56]

50. A study of the effects and potential adverse impacts of fentanyl buccal tablets (including Fentora) concluded that they were "generally safe and well tolerated, with self-reported

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of treatment with oral transmucosal fentanyl citrate (OTFC®, ACTIQ®)," *Pain Medicine* Vol. 8, No. 3 (2007): 281-88; Fine, Perry G et al., "Long-term safety and tolerability of fentanyl buccal tablet for the treatment of breakthrough pain in opioid-tolerant patients with chronic pain: an 18-month study," *Journal of Pain and Symptom Management* Vol. 40, No. 5 (2010): 747-60.

[53] Webster et al., "Fentanyl buccal tablet compared with immediate-release oxycodone for the management of breakthrough pain in opioid-tolerant patients with chronic cancer and noncancer pain: a randomized, double-blind, crossover study followed by a 12-week open-label phase to evaluate patient outcomes," *Pain Medicine* Vol. 14, No. 9 (2013): 1332-45.

[54] Ashburn et al., "The efficacy and safety of fentanyl buccal tablet compared with immediate-release oxycodone for the management of breakthrough pain in opioid-tolerant patients with chronic pain," *Anesthesia & Analgesia* Vol. 112, No. 3 (2011): 693-702.

[55] Taylor et al., "Impact of breakthrough pain on quality of life in patients with chronic, noncancer pain: Patient perceptions and effect of treatment with oral transmucosal fentanyl citrate (OTFC®, ACTIQ®)," *Pain Medicine* Vol. 8, No. 3 (2007): 281-88.

[56] Coluzzi, Paul H et al., "Breakthrough cancer pain: a randomized trial comparing oral transmucosal fentanyl citrate (OTFC®) and morphine sulfate immediate release (MSIR®)," *Pain* Vol. 91, No. 1-2 (2001): 123-30.

functional improvement observed in most of the opioid-tolerant patients with [breakthrough pain] in association with chronic noncancer pain."[57]

51. The labels for Actiq and Fentora state that these opioid medicines are indicated for the "management of breakthrough pain" in cancer patients who are already tolerant to opioid therapy for their underlying persistent cancer pain.[58] It may also be medically appropriate to prescribe OTFC medicines, such as Actiq and Fentora, for off-label purposes based on existing clinical practice guidelines, following a careful review of the patient's medical history, a physical examination, and a clear explanation of the risks.

52. The studies outlined above provide evidence that these medicines are effective in providing pain relief, and there are many cases where Actiq and Fentora might be particularly well-suited to addressing a patient's needs. For example, a spinal cord injury patient with a tracheotomy might benefit from a transdermal fentanyl patch, with Fentora or Actiq for breakthrough pain. Similarly, patients who do not tolerate oral medication (due to gastrointestinal upset, ulcers, difficulty swallowing, or other reasons) might also benefit. If the patient feels too sedated on the transdermal fentanyl patch, he or she might still benefit by using Fentora or Actiq alone. Withholding pain medication that is potentially medically appropriate could lead to unnecessary suffering on the part of the patient.[59]

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[57] Fine et al., "Long-term safety and tolerability of fentanyl buccal tablet for the treatment of breakthrough pain in opioid-tolerant patients with chronic pain: an 18-month study," *Journal of Pain and Symptom Management* Vol. 40, No. 5 (2010): 747-60.

[58] "Actiq Label, November 1998"; "Actiq Label, December 2016"; "Fentora Label, September 2006"; "Fentora Label, April 2017."

[59] *See* Deposition of Dr. Russell Portenoy, January 24, 2019 ("Portenoy Deposition"), at p. 304:4 to p.304:12, ("Q. So even today for the use of opioids to treat chronic pain associated with cancer is still less than where the

VII. OPINION #4: THE DECISION WHETHER TO PRESCRIBE AN OPIOID, INCLUDING ACTIQ OR FENTORA, SHOULD BE BASED ON AN INDIVIDUALIZED INQUIRY OF NUMEROUS PATIENT- AND PAIN-SPECIFIC FACTORS.

53. A prescriber's decision to include opioid medications in a treatment plan must be made on a patient-by-patient basis, after balancing the risks of harm with the potential benefits.

54. The decision to use short-acting opioids, including Actiq and Fentora, for the treatment of breakthrough pain is no different. The potential benefits include decreased pain intensity and improved physical and mental functioning, but at the risk of opioid-induced adverse events, possibly including increased risk of misuse, abuse, and diversion.[60]

55. Faced with these potential benefits and risks, health care providers deciding whether to prescribe Actiq and Fentora for any use (on-label or off-label) must exercise their independent professional, medical judgment. Such judgment may be based upon many different factors. These include, among other things, their medical training and experience; their specific experiences with Actiq and Fentora; their exposure to and understanding of the scientific literature regarding Actiq, Fentora, and similar opioid medication; their evaluation of the risk-benefit profile for the patient; the medical history of the patient including any history of substance abuse; the treatment history of the patient, including whether the patient has tried and failed alternative therapies, or whether the patient has had past success with Actiq and Fentora and is seeking a refill; direct input from the patient; appropriate monitoring for aberrant behaviors including urine drug

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scientific literature would suggest it needs to be; is that correct? A. Yes. Q. And you believe that is a detriment to patients who are suffering from pain who are not being adequately treated? A. Yes, I do.").

[60] "Actiq Label, December 2016"; "Fentora Label, April 2017."

screening and Prescription Drug Monitoring Programs (PDMP) review; review of adverse events; and influence by third party payers, such as insurance companies [61] Of course, over time, that judgment may shift, even for the same patient, depending on particular circumstances.

56. In my practice, the decision to recommend Actiq or Fentora for breakthrough pain in CNCP is based on my clinical judgment following a careful review of the patient's medical history and physical examination that lead to a clinical diagnosis and, in turn, the generation of an individualized treatment plan. Ongoing monitoring of patients is a vital component to managing pain in complex patients who require opioid therapy.

57. When assessing a patient for opioid therapy, physicians should be aware of the Centers for Disease Control (CDC) and State-specific guidelines. [62] It is my understanding that

[61] Plaintiffs' experts have recognized that "there are a lot" of factors other than marketing that influence doctors to prescribe medicines. Deposition of David Cutler, Ph.D., *In Re: National Prescription Opiate Litigation* MDL No. 2804, United States District Court for the Northern District of Ohio, Eastern Division, April 26, 2019, pp. 182-185 ("Q. [... H]ave you studied the different factors that motivate doctors to write prescriptions, or the variations in treatment among particular doctors? [...] A. [O]ne of the factors that enters into physicians' prescriptions is their own belief about effectiveness. [...] Q. Okay. Would you agree that physicians are also motivated by prescribing standards of care in terms of determining what types of prescriptions they write? A. In general there are a lot of influences on physicians. [...] Q. And patient preference also impacts a doctor's motivations to write prescriptions, right? [...] A. [... T]he economic literature does suggest that patient preferences are important, although the economic literature suggests that physician factors are far more important").

[62] For a summary of the CDC guidelines, *see* Dowell, Deborah, Tamara M. Haegerich, and Roger Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016," *Morbidity and Mortality Weekly Report* Vol. 65, No. 1 (2016): 1-49. The CDC issued an update in 2019 advising against the misapplication of the 2016 guidelines, see Centers for Disease Control and Prevention, "CDC Advises Against Misapplication of the Guideline for Prescribing Opioids for Chronic Pain," 2019, available at https://www.cdc.gov/media/releases/2019/s0424-advises-misapplication-guideline-prescribing-opioids.html, accessed April 26, 2019 ("CDC commends efforts by healthcare providers and systems, quality improvement organizations, payers, and states to improve opioid prescribing and reduce opioid misuse and overdose. However, some policies and practices that cite the Guideline are inconsistent with, and go beyond, its recommendations. [...] [P]olicies that mandate hard limits conflict with the Guideline's emphasis on individualized assessment of the benefits and risks of opioids given the specific circumstances and unique needs of each patient.").

Examples of state guidelines include: Governor's Cabinet Opiate Action Team, "Ohio Guideline for the Management of Acute Pain Outside of Emergency Departments," 2016, available at